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IMPACT OF PARTNER SUPPORT ON TIME TO FIRST TREATMENT FOR WOMEN WITH BREAST CANCER

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IMPACT OF PARTNER SUPPORT ON TIME TO FIRST TREATMENT FOR WOMEN WITH BREAST CANCER

CAPSTONE PROJECT PAPER

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ABSTRACT

Background: Treatment delays have been linked to decreased survival in women with breast cancer. Many women rely on their spouse or partner to provide support following breast cancer diagnosis. To date, little research has explored the effects of partner supportive behaviors on timely receipt of recommended cancer treatment and ultimately cancer survival.

Objective: To determine whether women identified as having lower partner support experience delays in time to first breast cancer treatment relative to women with highly supportive partners.

Methods: Women aged 18-79 who were diagnosed with incident and primary breast cancer within the past 12 months and included in the Kentucky Cancer Registry were recruited for the cohort study between November 2009 and December 2013. The new measure of Partner Supportive Behaviors in Cancer Care (5 item short form) was used to determine women's recall of partner supportive behaviors during and after cancer treatment and recovery. Unadjusted and adjusted linear regression, Kaplan-Meier, and Cox-Proportional Hazard modeling were used to determine the relationship between partner support and time to first treatment for women with breast cancer.

Results: Lower partner support was not significantly associated with longer time to first treatment for women with breast cancer, relative to women with highly supportive partners. Time to first treatment among 94 women with lower partner support was 22.2 days (SE: 1.9), compared to 21.7 days (SE: 1.5) for 144 women with moderate partner support, and 21.4 days (SE: 0.8) for women with highly supportive partners. The adjusted hazard ratio for those with lower partner support was 0.95 (95% CI: 0.76-1.18). This

pattern held for analyses of time to first cancer treatment independent of treatment type, by specific treatment (surgery and chemotherapy), and for analyses within early and late cancer stage.

Conclusions: To our knowledge, no other studies have examined the association between partner support and time to first cancer treatment. Future studies may consider the effect of other negative partner behaviors such as intimate partner violence or behaviors interfering with cancer care that may directly impact timely receipt of cancer treatment.

Keywords: breast cancer, treatment, partner support, delays

INTRODUCTION

Breast cancer remains the most common cancer diagnosis for women, despite the fact that incidence rates have stabilized from 2002 to 2011.[1] Breast cancer treatment options include surgery, chemotherapy, hormonal therapy, and radiation, with the majority of women receiving surgery as their first treatment.[2] While both screening and treatment options have played a role in the reduction of breast cancer mortality thus far, delays in treatment can negatively impact rate of survival.[3-5]

A meta-analysis of 38 studies showed a significant difference of survival between those with treatment delays less than 3 months and those with treatment delays of 3 to 6 months for women with breast cancer.[6] In a study focusing specifically on breast cancer in adolescents and young adults, a surgical delay of greater than 6 weeks influenced survival compared to those who received surgery closer to their diagnosis.[7] Because delays in receipt of first treatment have been shown to impact survival, this study focuses on delays in treatment among women with breast cancer; time to first treatment will be the primary outcome.

Many women look to their partner for the provision of social, emotional, and financial support following breast cancer diagnosis. Figueiredo et al found that 70% of women consider their partner as a confidant, and about 50% of these women identified their partner as their most important confidant.[8] The perception of partner unsupportive behaviors, such as changing the topic or being critical of coping strategies, can impact the well-being and distress of women with breast cancer, mostly due to the suppression of communication.[9] Similarly, the presence or the perception of interpersonal factors that hinder communication, known as social constraints, between patient and partner can lead

to decreased levels of both individual and relationship well-being, and lead to negative daily outcomes in the lives of breast cancer patients.[10]

While the previously mentioned studies have determined that unsupportive partner behaviors can prevent women from openly communicating or expressing concerns following breast cancer diagnosis, limited research exists looking for the effect of these behaviors on timely receipt of cancer care. In the present report, we will examine the relationship between unsupportive partner behaviors and time to first treatment for women with breast cancer. We hypothesize that a delay in therapy will be seen for women identified as having little to no support system, compared to women with a high level of partner support.

METHODS

Participant Recruitment

Women aged 18 to 79 diagnosed with an incident and primary case of breast cancer within the past 12 months were recruited from the Kentucky Cancer Registry (KCR) between November 2009 and December 2013. Researchers first reached out to physicians before contacting potential participants. Eligible women were then contacted by mail and given information on how to provide consent or decline participation. KCR made an additional attempt by phone to contact women who had not responded. Once consent was obtained, trained research staff at the University of Kentucky Survey Research Center (SRC) performed phone interviews to collect participant survey responses and demographic information. These interviews averaged 30 minutes.

Demographics

Demographic variables can be found in Table 1 for our total study population and for each level of partner support (low, moderate, or high). Demographic variables include age at diagnosis (mean ± standard error), the number of comorbidities (mean ± standard error), monthly income, classified as high or low, level of education, private insurance versus other insurance, stage at diagnosis, classified as stage 1/stage 2 (early stage) or stage 3/stage 4 (late stage), race, classified as Non-Hispanic White versus other, and smoking status, classified as current, former, never.

Measures

We defined our exposure, partner support, by creating 3 groups: low support, moderate support, or high support. Women were placed in 1 of the 3 groups based on their responses to 5 survey questions representing a new measure, Partner Supportive Behaviors in Cancer Care (PSB-C).[11] The questions were as follows: has your current partner or the person you were with when diagnosed gone to doctors' visits or appointments with you? Spent time with you when you were in the hospital? Been involved with your medical care, like asking your doctor questions or trying to learn more about your illness? Done something unexpected that would make you happy? Willingly made small sacrifices when you needed it or skipped a social activity to be with you? A Cronbach's alpha of 0.71 was calculated to measure the internal consistency of the 5 questions.

Dichotomous variables for each question were created based on survey responses and women received a 1 if their partners exhibited the behavior identified in the question

a little, some, or a lot, or a 0 if their partners did not exhibit the behavior identified in the question at all. The sum of these dichotomous variables allowed us to create the three groups of partner support. A PSB-C score of 1 to 3 points (out of a possible 5) placed women in the low support group, PSB-C score of 4 placed women in the moderate support group, and a PSB-C score of 5 placed the women in the high support group. For the purpose of our study, highly supportive partners serve as the reference group.

Our outcome, time to first treatment, was treated as a continuous variable, and is measured in days between diagnosis and receipt of first treatment. The data includes time to first treatment information for any type of treatment received, and also provides specific treatment information, such as time to first treatment based on specific treatment type. Everyone in the present study received treatment following breast cancer diagnosis.

Statistical Analysis

Comparisons were made across the 3 levels of partner support for all demographic variables. F-values were used to assess the differences between groups for continuous variables (age at diagnosis and number of comorbidities), and chi-square values were used for categorical variables (income, education, private insurance, stage at diagnosis, race, and smoking status,). Unadjusted and adjusted linear regression was performed to represent the effects of partner support on time to first treatment. The first adjustment, age and stage, was made based on a minimum sufficient set identified with a Directed Acyclic Graph (DAG) (Figure 1). The second adjustment, including age, stage, income, and comorbidities, was made based on the minimum sufficient DAG set and the

statistically significant relationships between income and comorbidities and partner support, as shown in Table 1.

Kaplan-Meier and Cox Proportional Hazard modeling were used to identify differences in time to first treatment based on level of partner support. Kaplan-Meier survival plots were created to determine the relationship between different levels of partner support and time to first treatment for all treatment types, within stage, and within types of treatment (surgery and chemotherapy). Unadjusted and adjusted hazard ratios were identified examining the relationship between partner support and time to first treatment for the following groups: time to first treatment for all treatment types, time to first treatment for those with early or late stage breast cancer, time to first treatment for those receiving surgery first, and time to first treatment for those receiving chemotherapy first. All statistical analysis was performed with SAS version 9.3.

RESULTS

A total of 4,628 eligible women were identified in Kentucky and 1,245 (26.9%) completed the telephone survey. Items measuring partner supportive behaviors were only asked of women in a relationship at cancer diagnosis; 886 were identified as being in a relationship (marriage or partnership). Our final study cohort included 844 women, after excluding women with missing values for stage, partner support, comorbidities, income, and time to first treatment (Figure 2). Among 844 women, 94 (11.1%) women were classified as having lower partner support (PSB-C of 1-3 of a maximum score of 5), 144 (17.1%) as having moderate partner support (PSB-C score=4), and 606 (71.8%) as having highly supportive partners (PSB-C score=5).

Table 1 provided data to determine demographic and cancer-related correlates of the three levels of partner supportive behaviors. Women with lower partner support were found to have more physical health comorbidities (p=0.01), lower monthly family income (p=0.005), and not to have private health insurance coverage (p=0.03) when compared to women with more supportive partners. Lower partner support was not associated with age, education, race, cancer stage at diagnosis, or smoking status. Based on this evaluation of correlates with partner support, only income, the number of comorbid conditions, and insurance coverage were significantly associated with partner support as our primary exposure.

Table 2, Figure 3, and Table 3 provide the results of the association between partner supportive behaviors and time to first cancer treatment using linear regression, Kaplan Meier curves, and Cox Proportional Hazards modeling, respectively. From Table 2, women identified as having lower partner support had a slightly higher time to first cancer treatment, at 22.2 days (SE: 1.9), while women with moderate partner support had a time to first cancer treatment of 21.7 days (SE: 1.5) and women with highly supportive partners had a time to first cancer treatment of 21.4 days (SE: 0.8). Differences in days to first cancer treatment by PSB-C groupings were not statistically significant for unadjusted or adjusted models.

Figure 3 represents Kaplan-Meier curves for the three PSB-C groups and time to first cancer treatment. Similar to the results of linear regression, no significant differences were observed for the association between partner support and time to first cancer treatment (p=0.93). Cox Proportional hazard ratios estimating the probability of experiencing delays in time to first cancer treatment potentially associated with lower

partner support are presented in Table 3. Again, lower partner support was not significantly associated with a longer time to first cancer treatment in unadjusted or adjusted hazard ratio models (adjusted HR: 0.95; 95% CI: 0.76, 1.18).

Kaplan Meier curves and Cox-Proportional Hazard modeling were repeated to examine the relationship between partner support and time to first treatment within early and late cancer stage at diagnosis (Figure 4, Table 4, Figure 5, and Table 5). Among the 233 women diagnosed at a later breast cancer stage, there was a suggestion that lower partner support may actually be associated with shorter time to first treatment, though not statistically significant (adjusted HR: 1.15, 95% CI: 0.73, 1.82) (Figure 5 and Table 5).

In Figure 6, Kaplan-Meier curves were provided for the three levels of PSB-C and time to first cancer treatment for women receiving surgery as their first treatment. Again, lower PSB-C scores were not significantly associated with longer time to first treatment (p=0.83). Table 6 provides the unadjusted and adjusted hazard ratios for partner support and time to treatment for women whose first treatment was surgery. Although representing a possible delay in time to first treatment for women with low partner support, there is no statistically significant association (adjusted HR: 0.91, 95% CI: 0.72, 1.14).

Finally, these same analyses were repeated for time to first cancer treatment for women who received chemotherapy as their first form of treatment. Similar to those diagnosed with later stage breast cancer, women with lower support receiving chemotherapy as their first form of treatment actually experienced a shorter time to first treatment, though not statistically significant (adjusted HR: 2.65; 95% CI: 0.74,

9.43)(Table 7). Limited power makes this analysis less reliable, as most women in our study received surgery as their first form of cancer treatment.

DISCUSSION

Lower PSB-C scores indicating fewer partner supportive behaviors were not significantly associated with longer time to first cancer treatment. Although a delay was observed based on unadjusted and adjusted linear regression and hazard ratios for most analyses, we cannot conclude that partner support is associated with longer time to first treatment for women with breast cancer. These findings were consistently not significant when adjusting for potential confounders, within cancer stage, and within specific cancer treatments (surgery and chemotherapy).

Our inability to find an association between partner support and time to first cancer treatment may be explained by a lack of power due to the majority of women having highly supportive partners (71.8%). Our exposure, partner support, may have been misclassified, as women may have struggled to acknowledge unsupportive partner behaviors, causing an inaccurate representation of the measure. Additionally, measuring partner support based solely on responses to 5 survey questions may not truly reflect the extent of unsupportive partner behaviors.

Manne et al concluded that there are associations between negative responses from a spouse and psychological outcomes for patients with cancer, regardless of the presence of positive spouse responses.[12] In our present study, it could be that partner behaviors not measured by our PSB-C variable elicit these negative responses between patient and spouse, even if the spouse is identified as supportive based on our scale.

Interestingly, a higher prevalence of violence has been identified among women diagnosed with cancer compared to other populations.[13] With our measure, PSB-C, we may have misclassified the more impactful partner behavior influences on time to first cancer treatment. Further investigation is needed to determine if the presence of other partner behaviors, such as intimate partner violence, play a role in the measurement of partner support and its overall impact on women's ability to obtain cancer care in a timely manner.

A strength of this study was the use of the Kentucky Cancer Registry to recruit eligible participants. The KCR includes all women diagnosed with biopsy confirmed cancer each year from 1995-the present. All 120 counties are included in KCR, thus representing a full census or population base of all cancer cases. It is possible that those agreeing to participate in this survey may have been of higher income or education. However, another study utilizing this dataset addressed this potential bias, with participation rates being higher for those living in Appalachian counties (29.9%) compared to those living in non-Appalachian counties (25.9%) ($p=0.01$). In this way, Appalachian residence serves as a proxy for lower income and less education since those variables were based on self-reporting and not provided through KCR. This finding supports the generalizability of our study sample to that of those included in KCR.

Our study analyzed the effect of partner unsupportive behaviors on time to first treatment for women with breast cancer; however, we know the majority of women received surgery as their first treatment (93%). Other studies have shown decreased survival for delays in receipt of chemotherapy following surgery for women with breast cancer.[14, 15] Future research may consider the impact of partner support on timely receipt

of adjuvant chemotherapy following surgery for women with breast cancer. Partner unsupportive behaviors may play a larger role in the recovery phase following surgery and leading up to first chemotherapy.

In conclusion, we observed that lower partner support was not significantly associated with longer time to first cancer treatment. Health care providers should consider directing their attention to other partner behaviors that may directly impact receipt of timely cancer care, such as intimate partner violence. Future studies should focus on improving the classification of partner unsupportive behaviors and seeing if this change in classification influences time to first treatment.

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BIOGRAPHICAL SKETCH

Laura Anne Cannon grew up in Lawrenceburg, Kentucky and graduated from Western Kentucky University with her B.S. in Chemistry. She was accepted into the University of Kentucky's College of Pharmacy in 2012 and began pursuing her PharmD in the fall of that year. She has always had an interest in global health, and decided to pursue the dual-degree PharmD/MPH program during the spring of 2013. Laura will graduate in May of 2016 and will be continuing her education at the University of Kentucky as a PGY1 Pharmacy Practice Resident for the 2016-2017 calendar year. Her current area of interest is oncology, which influenced her decision to pursue this Capstone topic. She is extremely thankful for the knowledge she has gained through the PharmD/MPH dual-degree, and is excited to see how it will play a role in her pharmacy practice moving forward.

Figure 1. Directed Acyclic Graph displaying potential confounding factors in determining the relationship between partner support and time to first treatment. Variables in red are considered the minimum sufficient set for adjusting for the relationship between exposure and outcome.

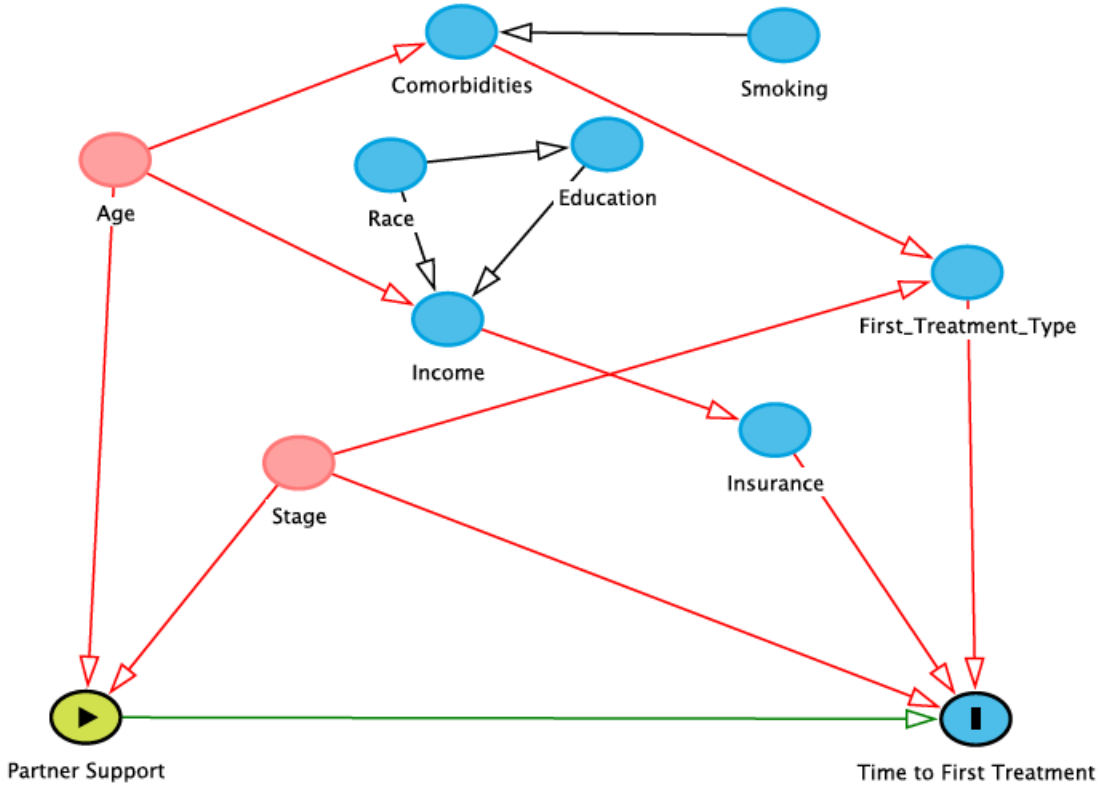

Figure 2. A flow chart representing study cohort participant selection.

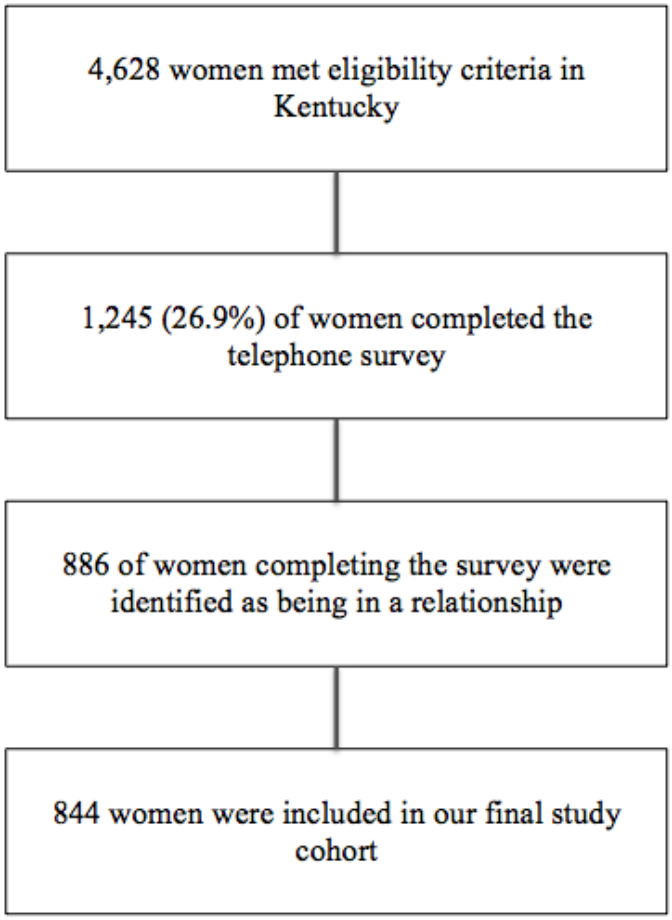

Table 1. Demographics for study cohort and for the 3 groups of partner support, including unadjusted analysis analyzing differences between the groups for each demographic variable.

	Total (N=844)	Low Support (N=94)	Moderate Support (N=144)	High Support (N=606)	DF	X^2 or F-value	*p-value*
Age at diagnosis (KCR) *Mean (SE)*	56.1 (0.3)	57.6 (1.0)	56.9 (0.8)	55.6 (0.4)	2, 841	2.24	0.11
Comorbidities* (Survey) *Mean (SE)*	1.5 (0.04)	1.9 (0.1)	1.4 (0.1)	1.5 (0.04)	2, 841	3.73	0.01
Income (Survey)							
High	513 (60.8%)	44 (46.8%)	83 (57.6%)	386 (63.7%)	2	10.4	0.005
Low	331 (39.2%)	50 (53.2%)	61 (42.4%)	220 (36.3%)			
Education (Survey)							
Less than high school	52 (6.2%)	5 (5.3%)	11 (7.6%)	36 (5.9%)			
High School/GED	287 (34.0%)	42 (44.7%)	47 (32.6%)	198 (32.7%)			
Some college	152 (18.0%)	13 (13.8%)	28 (19.4%)	111 (18.3%)	8	7.22	0.51
Bachelor Degree	110 (13.0%)	11 (11.7%)	21 (14.6%)	78 (12.9%)			
Post grad education/other	243 (28.8%)	23 (24.5%)	37 (25.7%)	183 (30.2%)			
Private Insurance (KCR)							
Yes	572 (67.8%)	54 (57.5%)	92 (63.9%)	426 (70.3%)	2	7.34	0.03
No	272 (32.2%)	40 (42.6%)	52 (36.1%)	180 (29.7%)			
Race (Survey)							
Non-Hispanic White	796 (94.3%)	90 (95.7%)	137 (95.1%)	569 (93.9%)	2	0.739	0.69
Other	48 (5.7%)	4 (4.3%)	7 (4.9%)	37 (6.1%)			
Stage at Diagnosis (KCR)							
Stage 1/Stage 2	611 (72.4%)	71 (75.5%)	107 (74.3%)	433 (71.5%)	2	0.99	0.61
Stage 3/Stage 4	233 (27.6%)	23 (24.5%)	37 (25.7%)	1753(28.6%)			
Smoking Status (Survey)							
Never Smoked	504 (59.7%)	45 (47.9%)	83 (57.6%)	376 (62.1%)			
Former Smoker	249 (29.5%)	34 (36.2%)	46 (31.9%)	169 (27.0%)	4	7.74	0.10
Current Smoker	91 (10.8%)	15 (16.0%)	15 (10.4%)	61 (10.1%)			

*average of comorbidities score from 0-6
KCR=Data available from the Kentucky Cancer Registry
Survey=Data available from telephone interviews with consenting women at least 12 months following diagnosis

Table 2. Unadjusted and adjusted linear regression comparing levels of partner support to number of days until first treatment.

	Mean Days to First Treatment (SE)					
	Unadjusted	*p-value*	Adjusted*	*p-value*	Adjusted**	*p-value*
Low Support	22.3 (1.8)	0.79	22.4 (1.9)	0.75	22.2 (1.9)	0.66
Moderate Support	21.9 (1.5)	0.98	21.9 (1.5)	0.95	21.7 (1.5)	0.82
High support	21.8 (0.7)	-----	21.7 (0.8)	-----	21.4 (0.8)	-----

*adjusted for age at diagnosis and stage

**adjusted for age at diagnosis, stage, comorbidities, and income

Figure 3. Kaplan-Meier estimate comparing levels of partner support to the number of days between diagnosis and treatment (low support=0, moderate support=1, high support=2), p=0.926.

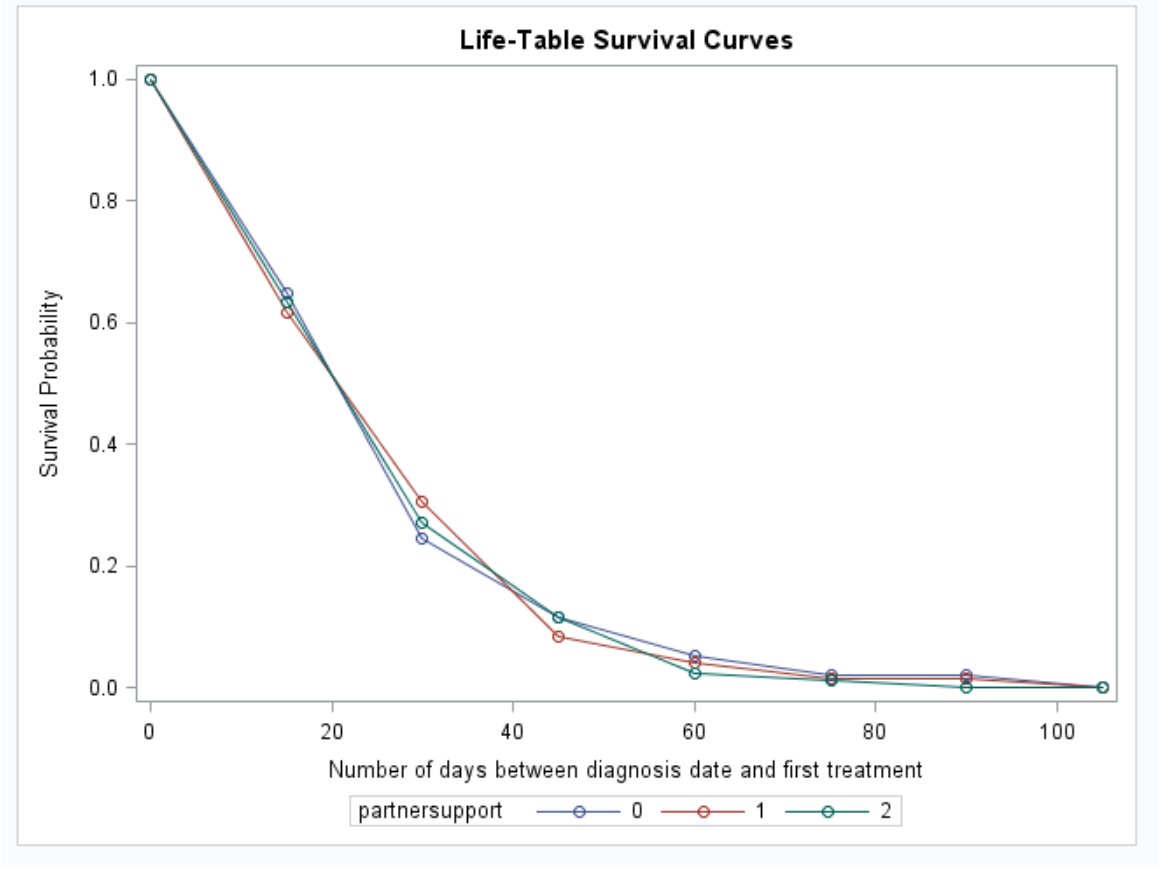

Table 3. Unadjusted and adjusted cox proportional hazards model comparing levels of partner support to number of days until first treatment.

	Hazard Ratio (95% Confidence Interval)		
	Unadjusted	Adjusted*	Adjusted**
Low Support	0.96 (0.77, 1.19)	0.95 (0.77, 1.19)	0.95 (0.76, 1.18)
Moderate Support	0.99 (0.83, 1.19)	0.98 (0.82, 1.18)	0.97 (0.81, 1.16)
High support (*ref*)	-----	-----	-----

*adjusted for age at diagnosis and stage
**adjusted for age at diagnosis, stage, comorbidities, and income

Figure 4. Kaplan-Meier estimate comparing levels of partner support to the number of days between diagnosis and treatment for women diagnosed with early stage breast cancer (low support=0, moderate support=1, high support=2), p=0.415.

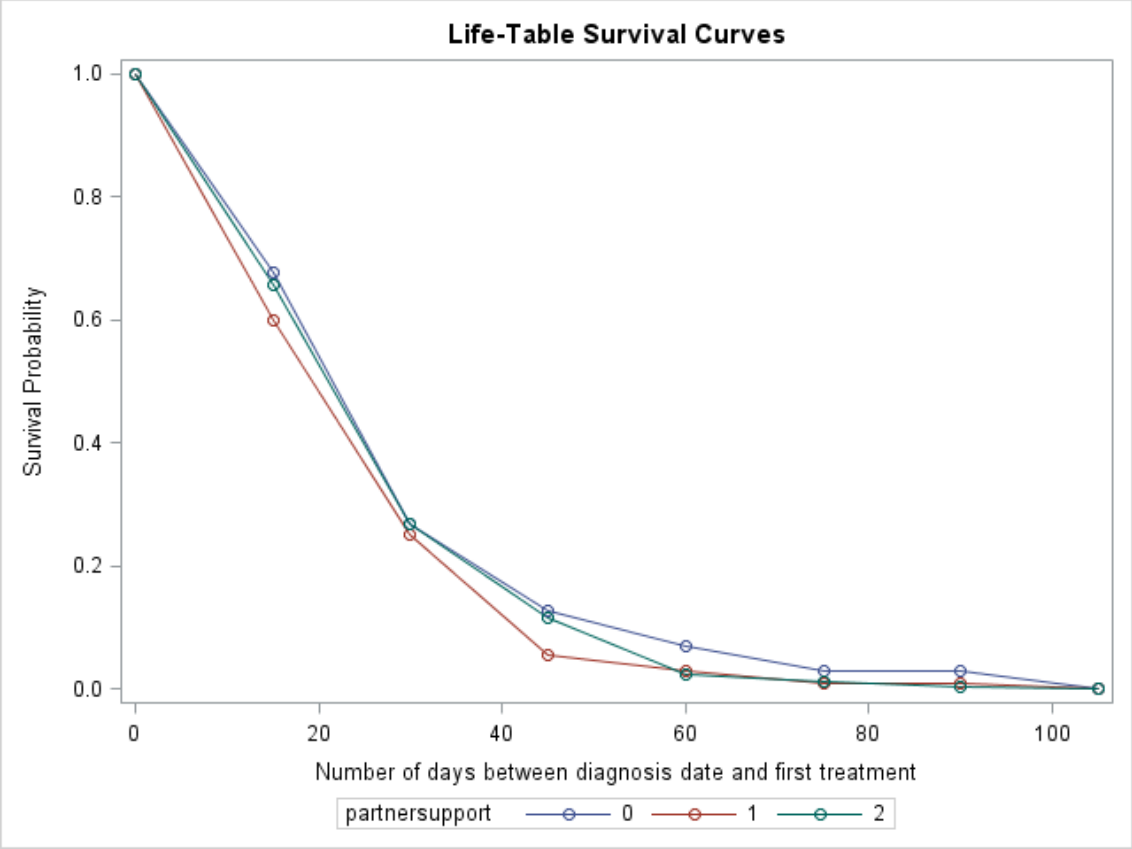

Table 4. Unadjusted and adjusted cox proportional hazards model comparing levels of partner support to number of days until first treatment for those diagnosed as stage 1 or stage 2 (early stage).

Early Stage (N=611)	Hazard Ratio (95% Confidence Interval)		
	Unadjusted	Adjusted*	Adjusted**
Low Support	0.93 (0.72, 1.20)	0.92 (0.72, 1.19)	0.91 (0.71, 1.18)
Moderate Support	1.12 (0.91, 1.38)	1.11 (0.90, 1.38)	1.09 (0.88, 1.35)
High support (*ref*)	-----	-----	-----

*adjusted for age
**adjusted for age at diagnosis, comorbidities, and income

Figure 5. Kaplan-Meier estimate comparing levels of partner support to the number of days between diagnosis and treatment for women diagnosed with late stage breast cancer (low support=0, moderate support=1, high support=2), p=0.196.

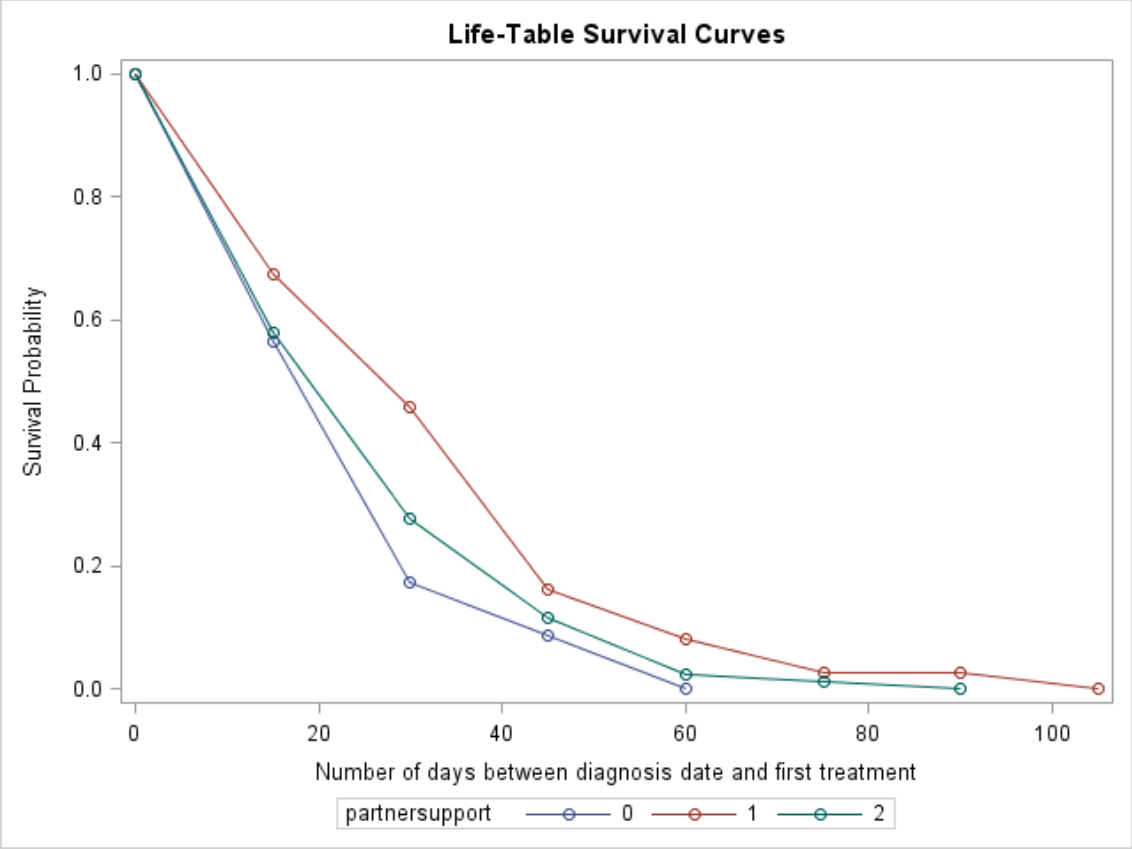

Table 5. Unadjusted and adjusted cox proportional hazards model comparing levels of partner support to number of days until first treatment for those diagnosed as stage 3 or stage 4 (late stage).

Late Stage (N=233)	Hazard Ratio (95% Confidence Interval)		
	Unadjusted	Adjusted*	Adjusted**
Low Support	1.10 (0.71, 1.70)	1.11 (0.71, 1.72)	1.15 (0.73, 1.82)
Moderate Support	0.74 (0.52, 1.07)	0.75 (0.52, 1.08)	0.74 (0.51, 1.06)
High support (*ref*)	-----	-----	-----

*adjusted for age at diagnosis
**adjusted for age at diagnosis, comorbidities, and income

Figure 6. Kaplan-Meier estimate comparing levels of partner support to the number of days between diagnosis and treatment for women receiving surgery as their first treatment (low support=0, moderate support=1, high support=2), p=0.833.

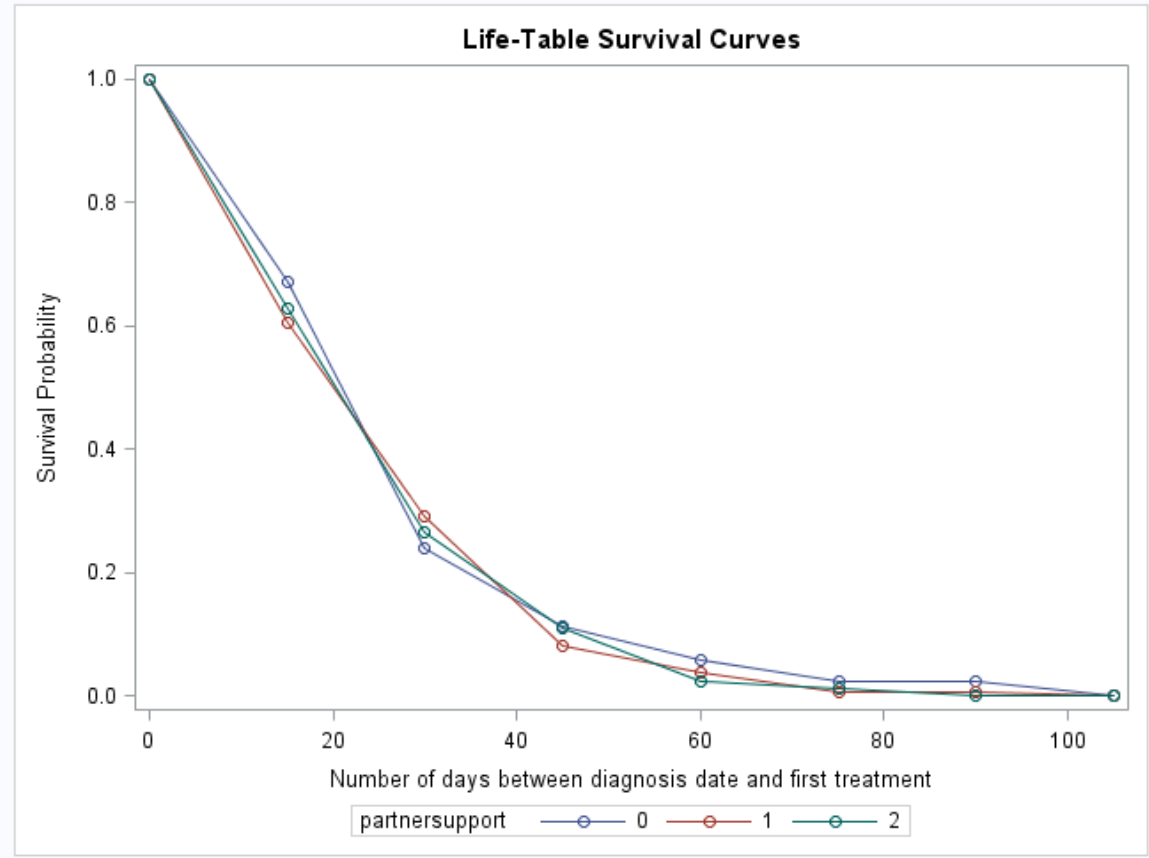

Table 6. Unadjusted and adjusted cox proportional hazards model comparing levels of partner support to number of days until first treatment for those receiving surgery as their first treatment.

Surgery (N=785)	Hazard Ratio (95% Confidence Interval)		
	Unadjusted	Adjusted*	Adjusted**
Low Support	0.94 (0.75, 1.18)	0.93 (0.74, 1.17)	0.91 (0.72, 1.14)
Moderate Support	1.01 (0.83, 1.21)	1.00 (0.83, 1.21)	0.98 (0.81, 1.19)
High support (*ref*)	-----	-----	-----

*adjusted for age
**adjusted for age at diagnosis, comorbidities, and income

Figure 7. Kaplan-Meier estimate comparing levels of partner support to the number of days between diagnosis and treatment for women receiving chemotherapy as their first treatment (low support=0, moderate support=1, high support=2), p=0.536.

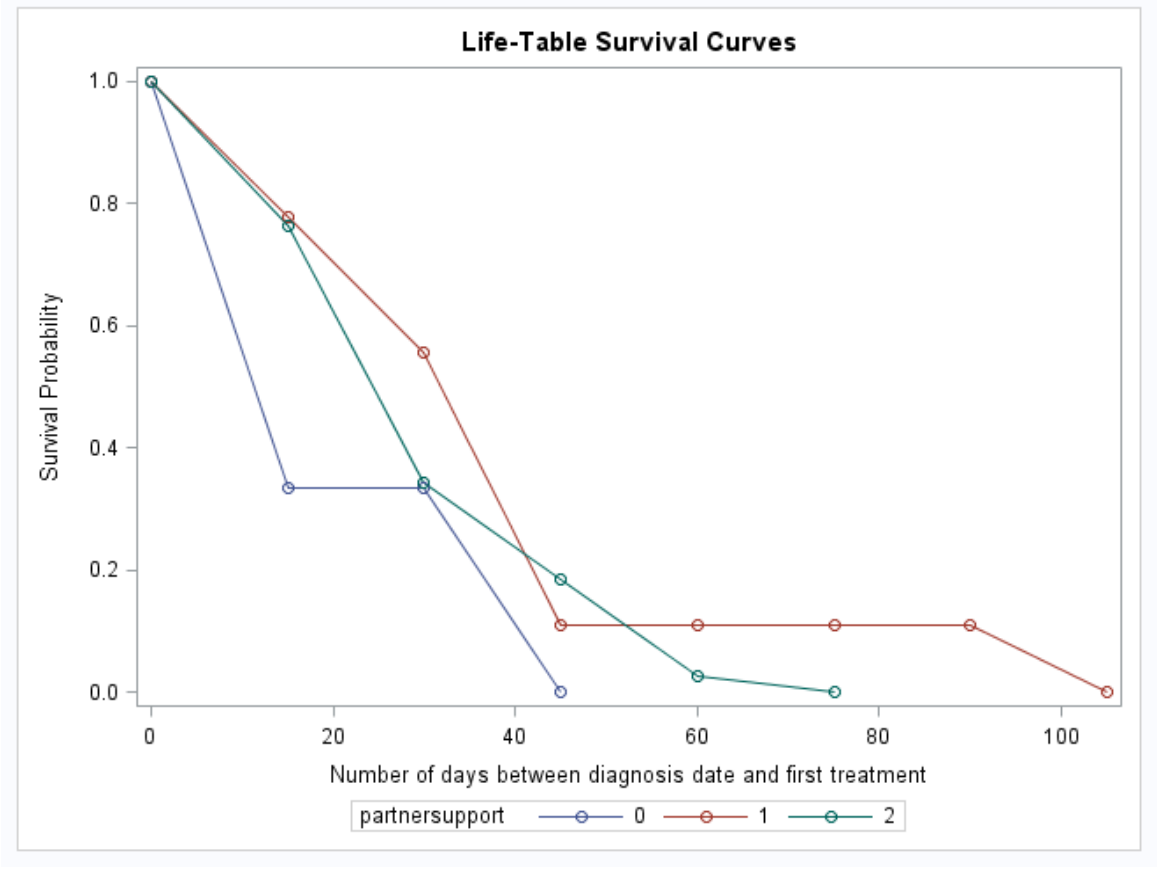

Table 7. Unadjusted and adjusted cox proportional hazards model comparing levels of partner support to number of days until first treatment for those receiving chemotherapy as their first treatment.

Chemotherapy (N=50)	Hazard Ratio (95% Confidence Interval)		
	Unadjusted	Adjusted*	Adjusted**
Low Support	1.69 (0.51, 5.54)	1.75 (0.53, 5.76)	2.65 (0.74, 9.43)
Moderate Support	0.81 (0.37, 1.75)	0.98 (0.43, 2.21)	0.83 (0.35, 1.95)
High support (*ref*)	-----	-----	-----

*adjusted for age

**adjusted for age at diagnosis, comorbidities, and income

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